REMARKS

Claims 17, 19, and 20 have been amended to depend upon a pending claim. This amendment is fully supported by the specification and original claims and do not introduce any new matter. Claims 1, 13, 17-20, and 22-24 are currently withdrawn from consideration. Claims 1, 13, 17-20, and 22-34 are pending.

I. Priority

Applicants thank the Examiner for acknowledging Applicants' claims to domestic priority under 35 U.S.C. § 119(e). *See* Paper No. 1126, page 5, second full paragraph. In response to the Examiner's request for identification of the priority document that describes SEQ ID NO:105, Applicants direct the Examiner to Provisional Application No. 60/054,212, filed July 30, 1997. As noted in Table 1, row 5, page 45 of Application No. 60/054,212, gene 4 corresponds to the HAUAQ39 cDNA contained within ATCC Deposit No. 209145 and SEQ ID NO:105. In addition, Application No. 60/054,212 describes gene 4 on page 47, lines 22 to 35.

Applicants also submit herewith Exhibit A, an alignment of SEQ ID NO:12, the polynucleotide sequence corresponding to gene 4 of the instant Application, Serial No. 09/820,649, with SEQ ID NO:4, the polynucleotide sequence corresponding to gene 4 of priority Application No. 60/054,212. Exhibit A shows that gene 4, which corresponds to the HAUAQ39 cDNA contained within ATCC Deposit No. 209145, is the same in both the instant application and priority Application No. 60/054,212.

In light of the support provided above, Applicants submit that the polypeptide encoded by the HAUAQ39 cDNA contained within ATCC Deposit No. 209145 and SEQ ID NO:105 are entitled to a priority date of July 30, 1997.

II. Utility/Enablement Rejections Under 35 U.S.C. §§ 101/112

The Examiner has rejected claims 25-35 under 35 U.S.C. § 101, for allegedly lacking a specific or substantial or well-established utility. In particular, the Examiner alleges,

> ...the specification fails to assert any utility for the claimed polypeptides or the encoded proteins and neither the specification as filed, nor any art of record discloses or suggests any activity for the claimed polypeptides or the

> encoded proteins such that another non-asserted utility would be well established.

Paper No. 1126, page 5, fourth full paragraph. Applicants respectfully disagree and traverse.

In order to find that an asserted utility is not specific and substantial or well-established, the burden is on the Examiner to make a *prima facie* showing that it is more likely than not that a person of ordinary skill in the art would not consider any utility asserted by the Applicant to be specific and substantial or well-established. *See*, M.P.E.P. § 2107.02(IV); and the Utility Examination Guidelines at 1098, col. 3. Such a *prima facie* showing must contain (1) an explanation that clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is not both specific and substantial nor well-established; (2) support for factual finding relied upon in reaching this conclusion; and (3) evaluation of all relevant evidence of record, including utilities taught in the closest prior art. *See id.*

Applicants contend that the Examiner has provided no evidence or support that (1) the logic underlying Applicants' assertions of utility is seriously flawed, (2) the facts upon which Applicants base the assertions of utility are inconsistent with the logic underlying the assertions, or (3) the statements of asserted utility in the present application would be considered "false" by a person of ordinary skill in the art. The Examiner has simply provided generalized statements that the instant specification does not provide any evidence that the claimed polypeptide is involved in any of utilities disclosed in the specification. (*See*, Paper No.1126, pages 5-8).

With regard to evaluating if an invention has a "specific" utility, the M.P.E.P. § 2107.01 on page 2100-32 states that,

> Office personnel should distinguish between situations where an applicant has disclosed a specific use for or application of the invention and situations where the applicant merely indicates that the invention may prove useful without identifying with specificity why it is considered useful. For example, indicating that a compound may be useful in treating unspecified disorders...would not be sufficient to define a specific utility for the compound....Contrast the situation where an Applicant discloses a specific biological activity and reasonably correlates that activity to a disease condition. Assertions falling within [this] category are sufficient to identify a specific utility for the invention.

With regard to evaluating if an invention has a "substantial" utility, the M.P.E.P. states that if a utility has a "real-world" use it should be considered to be substantial. In particular, M.P.E.P. § 2107.01 at page 2100-33 states "any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, as least with regard to defining a 'substantial' utility."

Contrary to the Examiner's arguments, Applicants contend that the specification sets forth a specific and substantial utility for the present invention. For example, the specification describes how the polypeptides of the invention are primarily expressed in a variety of cell types including muscle and bone. *See*, specification, for example, at page 13, lines 31-32. The specification further states that the polypeptides of the invention may be useful, for example, in the diagnosis and/or treatment of disease and conditions, including, but not limited to, "osteoporosis or any of a variety of diseases that involve wasting of bone or muscle." *See*, specification, at page 14, lines 4-5. Applicants contend that one of skill in the art would clearly find this asserted utility to be specific. In addition, since the diagnosis and/or treatment of such specific diseases is certainly a "real-world" use, Applicants contend that the skilled artisan would also find the assertion of utility to be substantial.

With regard to the utility of the differential expression of the polypeptide in muscle and bone, the Examiner alleges that the "...specification fails to provide any description of how to use such tissue or cells for expression or how such expression would have been assessed." *See* Paper No.1126, page 6, first paragraph, lines 9-11. Applicants respectfully point out that techniques for detecting the differential expression of a polynucleotide or polypeptide from a tissue or cell were well known in the art at the time of filing and are described in the specification, for example, on pages 178 and 207-208.

In view of the reasons given above, Applicants assert that one of ordinary skill in the art would consider Applicants' asserted utility of the invention, to be *specific and substantial* and clearly would have no basis for considering these asserted utilities to be "false." Accordingly, Applicants respectfully request the Examiner reconsider and withdraw the rejection of claims 25-34 under 35 U.S.C. § 101 for alleged lack of utility.

III. <u>Rejections Under 35 U.S.C. § 112, First Paragraph</u>

a. The Examiner has rejected claims 25-34, under 35 U.S.C. § 112, first paragraph,

for lack of enablement. *See* Paper No.1126, page 9, first paragraph. More particularly, the Examiner states that the claimed invention is allegedly not supported by either a specific and substantial or well-established utility, thus one skilled in the art would not know how to use the claimed invention without undue experimentation. Applicants respectfully disagree and traverse.

For the reasons discussed in the section above, the claimed invention is supported by a credible, specific and substantial utility. Since the Examiner "should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on 'lack of utility' basis unless a 35 U.S.C. § 101 rejection is proper." M.P.E.P. § 2107.01(IV) at 2100-36, Applicants respectfully request the Examiner reconsider and withdraw the rejection of claims 25-34 under 35 U.S.C. § 112, first paragraph.

b. The Examiner has objected to the specification and rejected claims 30-34 under 35 U.S.C. § 112, first paragraph, as allegedly failing to provide an adequate written description, enablement and best mode for practicing the claimed invention. Paper No. 1126, page 9, second full paragraph.

More particularly, the Examiner asserts that the specification is objected to because while the biological material used in the claimed process is a microorganism clone deposited with the ATCC, since the clone is essential to the practice of the claimed invention it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. (*See* page 9, third full paragraph of Paper No. 1126).

While Applicants assert that the instant specification provides adequate assurances that the ATCC deposit was made pursuant to the terms of the Budapest Treaty (*see* page 3, lines 35-37), a fact also recognized by the Examiner (*see* page 10, first full paragraph of Paper No. 1126), a statement concerning the public availability of the deposited cDNA clone, signed by Applicants' attorney, is enclosed. Thus, Applicants respectfully submit that this aspect of the objection has been overcome.

Further, the Examiner objects to Example 1, which describes the isolation of a given cDNA invention from an ATCC deposit, for the following reasons:

> ...applicants have apparently incorporated specific references into the specification does not eliminate the issue

> of public availability and permanence as the **vectors cited in the references and the references per se do not indicate, public availability of the starting materials** in as much as the biological materials mentioned in a publication may be proprietary and not publicly available.

Paper No.1126, page 9, fourth full paragraph (emphasis added).

Applicants respectfully disagree and traverse. Applicants respectfully submit that the "public availability and permanence" of the vectors that were used for isolating the cDNA inventions is not material to 35 U.S.C. § 112, first paragraph, because all that one of ordinary skill in the art would need to isolate a specific cDNA plasmid from a mixture of cDNA plasmids is the identity of the inserted cDNA and an appropriate cloning method. *See* the present specification at page 176, lines 11-14, and Table 1 at pages 127 to 138. Nevertheless, Applicants point out that the sequences of all of the vectors referred to on page 176 can be obtained from numerous publicly accessible databases, e.g., VectorDB (http://genome-www2.stanford.edu/vectordb/), Integrated Molecular Analysis of Genomes and their Expression, or the I.M.A.G.E. consortium (http://image.llnl.gov/), and NCBI Entrez nucleotide (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Nucleotide). Thus, Applicants respectfully request reconsideration and withdrawal of this aspect of the specification objection and claim rejection.

The Examiner further objects to Example 1 for the following reasons:

> It is apparent that the claimed clone is essential to the claimed invention and the deposit is necessary for an adequate written description, enablement, and best mode for the claimed invention, because the specification lacks a specific description or demonstration of hundred percent reproducibility of the claimed protein from the deposit. Because of the overlapping sequences the deposit is not 100% reproducible. Specification indicates in Example 1 (page 176, lines 7-10) that typically each ATCC deposit sample cited in Table 1 comprises a mixture of approximately equal amounts (by weight) of about 50 plasmid DNAs, each containing a different cDNA clone; but such a deposit sample may include plasmids for more or less than 50 cDNA clones, up to about 500 cDNA clones. However, Example 1 only gives a generic description of isolation of a selected clone from the deposited sample, it fails to demonstrate the selection of a single clone from the mixture of cDNA clones from the deposit. Thus, the specification does not disclose a repeatable process to obtain the claimed clone from the deposit.

Paper No.1126, page 9, fifth full paragraph to page 10 first paragraph. Applicants respectfully disagree and traverse.

As a preliminary matter, Applicants point out that the meaning of the phrase "100% reproducibility" in the first two sentences of the quote above is unclear, and therefore, this aspect of the Examiner's rejection is unclear to Applicants. Nevertheless, Applicants respectfully submit that independent of the particular vector(s), or cDNA inserts present in a given deposit, one of ordinary skill in the art could have employed either of the methods described in Example 1 of the present specification to isolate a cDNA of interest. *See* page 176, second full paragraph to the paragraph bridging pages 176 and 177. For example, by transforming the DNA contained within ATCC Deposit No. 209145 into host cells, one of ordinary skill in the art could generate a population of isolated colonies each containing a particular cDNA plasmid. Following transformation, screening with an oligonucleotide complementary to one of Applicant's disclosed sequences would enable easy identification of the isolated transformant(s) containing the cDNA plasmid of interest. Accordingly, Applicants respectfully request reconsideration and withdrawal of this aspect of the specification objection and claim rejection.

Finally, Applicants have attached herewith Exhibit B, a photocopy of the receipt of the ATCC deposit as requested by the Examiner in Paper No. 1126, on page 10, first full paragraph. In view of Exhibit B, and the statement regarding availability of the deposited clone, Applicants believe the Examiner's concerns have been fully addressed.

In light of the reasoning given above, Applicants respectfully request that the Examiner's objection to the specification and rejection of claims 30-34 under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

IV. <u>Rejection Under 35 U.S.C. § 102(b)</u>

The Examiner has rejected claims 27 and 32 under 35 U.S.C. § 102(b), as allegedly anticipated by GenEmbl entry HS434P1B which teaches a KDEL receptor polypeptide 99.2% identical to amino acid residues 2-220 of SEQ ID NO:105. *See* Paper No. 1126, page 10, fourth full paragraph. Applicants respectfully disagree and traverse.

Applicants note that GenEmbl entry HS434P1B was submitted on December 22, 1998. However, as described in Part I above, the present application claims priority under 35 U.S.C. § 119(e) to U.S. Provisional Application No. 60/054,212, filed July 30, 1997. Therefore, because the priority date of the present application predates the submission date

of the GenEmbl entry HS434P1B, said GenEmbl entry is not properly prior art against the rejected claims, thus the rejection of claims 27 and 32 under 35 U.S.C. § 102(b) is moot. Accordingly, Applicants respectfully request that rejection of claims 27 and 32 under 35 U.S.C. § 102 be withdrawn.

Conclusion

Applicants respectfully request that the above-made remarks be made of record in the file history of the instant application. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the examination of this application. If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the fee should also be charged to our Deposit Account.

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Respectfully submitted,

By _____
Janet M. Martineau
Registration No.: 46,903
HUMAN GENOME SCIENCES, INC.
14200 Shady Grove Road
Rockville, Maryland 20850
(301) 315-2723

KKH/JMM/ZSS/vsr